STIC Search

9/5/02

```
show files
File 155:MEDLINE(R) 1966-2002/Sep W1
File   5:Biosis Previews(R) 1969-2002/Aug W4
         (c) 2002 BIOSIS
File 315:ChemEng & Biotec Abs 1970-2002/Jul
         (c) 2002 DECHEMA
File  73:EMBASE 1974-2002/Aug W4
         (c) 2002 Elsevier Science B.V.
?ds

Set     Items   Description
S1     323999   VACCIN?
S2     146007   ADJUVANT? ?
S3       8096   IMMUNOSTIMULAN? OR IMMUNO()STIMULAN?
S4        856   ALUMINUM(2N)SALT? ?
S5       4163   LIPID A
S6      10012   LIPID()A
S7      26011   ACYLAT?
S8       1809   MONOPHOSPHORYL?
S9     339449   PHOSPHORYL?
S10   1229663   ANTIGEN? ?
S11    152282   HEPATITIS?(3N)(A OR B)
S12         1   ALUMINUM (3N) PHOSPATE? ?
S13     10075   ALUMINUM (3N) HYDROXIDE? ?
S14      5319   ALUM
S15    154044   ADSOR?
S16    312909   PARTICLE? ?
S17    595482   SEPARATE?
S18        64   AU=GARCON N? OR AU=GARCON, N?
S19         4   S18 AND S16
S20         6   S18 AND S5
S21        10   S19 OR S20
S22        14   S18 AND S6
S23        18   S21 OR S22
S24      1093   (S5 OR S6) (5N) S8
S25         5   S24 (5N) S7
S26        25   S24 AND S16
S27        16   RD S26 (unique items)
S28        36   S24 AND S15
S29      2654   ALUMINUM(3N)PHOSPHATE? ?
S30      2709   S2 AND (S13 OR S14 OR S29)
S31       404   S30 (5N)(S15 OR S16)
S32         9   S31 (5N) FREE?
S33        26   S31 AND (S5 OR S6)
S34        63   S31 AND S11
S35       158   S23 OR S25 OR S27 OR S28 OR S32 OR S33 OR S34
S36     18718   IMMUNOSTIMULAT? OR IMMUNO()STIMULAT?
S37        93   RD S35 (unique items)
S38        41   S37 AND S11
S39         6   S37 AND S17
S40        87   S37 NOT S39
S41         7   S40 AND ALLERG?
S42        80   S40 NOT S41
S43         9   S42 AND S18
S44        71   S42 NOT S43
S45        18   S44 AND ((S10 OR S11)(5N)(S15 OR S16))
S46         7   S44 AND ((S5 OR S6)(5N) (S15 OR S16))
```

S47 34 S43 OR S45 OR S46
S48 46 S44 NOT S47
S49 9 S48 AND (COVALEN? OR BOUND OR BIND?)
S50 43 S47 OR S49
?t 50/7/all

50/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12843840 21418178 PMID: 11527151
Inducible expression of the alpha2-macroglobulin signaling receptor in response to antigenic stimulation: a study of second messenger generation.
Bhattacharjee G; Misra U K; Gawdi G; Cianciolo G; Pizzo S V
Department of Pathology, Duke University Medical Center, Durham, North Carolina 27710, USA.
Journal of cellular biochemistry (United States) 2001, 82 (2) p260-70, ISSN 0730-2312 Journal Code: 8205768
Contract/Grant No.: HL-24066; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Thioglycollate (TG)-elicited murine, peritoneal macrophages express two receptors for activated forms of the proteinase inhibitor alpha2-macroglobulin (alpha2M*)--namely, the low density lipoprotein receptor-related protein (LRP) and the alpha2M signaling receptor (alpha2MSR). We now report that resident peritoneal macrophages express only 400+/-50 alpha2MSR receptors/cell compared to 5000+/-500 receptor/TG-elicited macrophage. By contrast, LRP expression is only 2-2.5-fold greater on elicited cells. The low level of alpha2MSR expression by resident cells is insufficient to trigger signal transduction in contrast to TG-elicited cells which when exposed to alpha2M* demonstrate a rapid rise in inositol 1,4,5-trisphosphate and a concomitant increase in cytosolic free Ca2+. We then studied a variety of preparations injected subcutaneously for their ability to upregulate alpha2MSR. Macroaggregated bovine serum albumin (macroBSA) injection upregulated alpha2MSR and triggered signaling responses by splenic macrophages. Nonaggregated BSA injection alone or in the presence of alum, by contrast, did not alter alpha2MSR expression. Recombivax (hepatitis B antigen adsorbed to alum) injection also upregulated alpha2MSR on splenic macrophages while the alum carrier had no effect. We conclude that macrophage alpha2M* receptors are inducible and their expression may be regulated, in part, by potential antigens.
Record Date Created: 20010830

50/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12782522 21454083 PMID: 11567766
Targeting polymerised liposome vaccine carriers to intestinal M cells.
Clark M A; Blair H; Liang L; Brey R N; Brayden D; Hirst B H
Department of Physiological Sciences, Medical School, University of Newcastle, NE2 4HH, Newcastle upon Tyne, UK.
Vaccine (England) Oct 12 2001, 20 (1-2) p208-17, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Due to their transcytotic capability, intestinal M cells may represent an efficient potential route for oral vaccine delivery. We previously demonstrated that the lectin Ulex europaeus agglutinin 1 (UEA1, specific for alpha-L-fucose residues) selectively binds to mouse Peyer's patch M cells and targets 0.5 microm polystyrene microparticles to these cells. Using a gut loop model we now demonstrate that covalently -membrane- bound UEA1 similarly targets polymerised liposomes (Orasomes, approximately 200 nm diameter), potential biocompatable oral vaccine delivery vehicles, to mouse M cells. Targeting was inhibited by alpha-L-fucose while the co-entrapped adjuvant, monophosphoryl Lipid A (MPL), failed to exert any detrimental effect on UEA1-mediated M cell targeting. Lectin-mediated M cell targeting may thus permit the efficacy of mucosal vaccines to be enhanced if cellular relationship between particle binding and immune outcome can be established.

Record Date Created: 20010924

50/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12695041 21427778 PMID: 11535326

Induction of cross clade reactive specific antibodies in mice by conjugates of HGP-30 (peptide analog of HIV-1(SF2) p17) and peptide segments of human beta-2-microglobulin or MHC II beta chain.

Zimmerman D H; Lloyd J P; Heisey D; Winship M D; Siwek M; Talor E; Sarin P S

CEL-SCI Corporation, 8229 Boone Blvd, Suite 802, Vienna, VA 22182, USA. dzimmerman@cel-sci.com

Vaccine (England) Sep 14 2001, 19 (32) p4750-9, ISSN 0264-410X
Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

HGP-30, a 30 amino acid synthetic peptide homologous to a conserved region of HIV-1(SF2) p17 (aa86-115), has previously been shown to elicit both cellular and humoral immune responses when conjugated to KLH and adsorbed to alum . However, the free HGP-30 peptide is not immunogenic in animals. In order to improve the immunogenicity of HGP-30, peptide conjugates consisting of a modified HGP-30 sequence (m-HGP-30/aa82-111) and a peptide segment, residues 38-50, of the MHC I accessory molecule, human beta-2-microglobulin (beta-2-M), referred to as Peptide J, or a peptide from the MHC II beta chain (peptide G) were evaluated in mice. The effects of carriers and adjuvants on serum antibody titers, specificities to various HIV-1 clade peptides similar to HGP-30 and isotype patterns were examined. Peptides J or especially G conjugated to modified-HGP-30 (LEAPS 102 and LEAPS 101, respectively) generated comparable or better immune responses to modified HGP-30 than KLH conjugates as judged by the induction of: (1) similar antibody titers; (2) broader HIV clade antigen binding ; and (3) antibody isotype response patterns indicative of a TH1 pathway (i.e. increased amounts of IgG2a and IgG2b antibodies). The ISA 51 and MPL(R)-SE adjuvants induced higher antibody responses than alum, with the ISA 51 being more potent. Immune responses to LEAPS 102, as compared to LEAPS 101, were weaker and slower to develop as determined by antibody

titers and cross clade reactivity of the antibodies induced. Compared to KLH conjugates which induced significant anti-KLH antibody titers, minimal antibody responses were observed to peptide G, the more immunogenic conjugate, and peptide J. These results suggest that modified HGP-30 L.E.A.P.S. constructs may be useful as HIV vaccine candidates for preferential induction of TH1 directed cell mediated immune responses.
Record Date Created: 20010905

50/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11121142 21127277 PMID: 11228376
Monophosphoryl lipid A adjuvant reverses a principal histologic parameter of formalin-inactivated respiratory syncytial virus vaccine-induced disease.
Prince G A; Denamur F; Deschamps M; Garcon N ; Prieels J P; Slaoui M; Thiriart C; Porter D D
Virion Systems Inc., Rockville, MD 20850, USA. gprince@erols.com
Vaccine (England) Feb 28 2001, 19 (15-16) p2048-54, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The mechanisms by which administration of a formalin-inactivated respiratory syncytial virus vaccine resulted in enhanced disease among children after they later became naturally infected with the virus remains largely undefined. After immunization and live virus challenge, the cotton rat demonstrated the histopathologic marker of the enhanced disease, polymorphonuclear leukocyte infiltration of lung alveolar spaces. We now report that immunization with formalin-inactivated vaccine formulated with the adjuvant, 3-deacylated monophosphoryl lipid A , dramatically reduces or eliminates the polymorphonuclear leukocyte infiltration within the alveoli of cotton rats post-challenge. We suggest, that this or similar adjuvants may be beneficial components of candidate non-replicating respiratory syncytial virus vaccines, whose development has been hampered by safety concerns.
Record Date Created: 20010306

50/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11098088 21108971 PMID: 11166900
Detoxification of endotoxin by aluminum hydroxide adjuvant.
Shi Y; HogenEsch H; Regnier F E; Hem S L
Department of Industrial and Physical Pharmacy, Purdue University, West Lafayette, IN 47907, USA.
Vaccine (England) Feb 8 2001, 19 (13-14) p1747-52, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Langmuir adsorption isotherms of endotoxin and aluminum-containing adjuvants at pH 7.4 and 25 degrees C revealed that aluminum hydroxide

adjuvant has a greater adsorption capacity (283 microg/mg Al) and adsorption coefficient (1.3x10(4) ml/miccrog) than aluminum phosphate adjuvant (3.0 microg/mg Al, 0.20 ml/microg). The difference in endotoxin adsorption was related to two adsorption mechanisms: electrostatic attraction and covalent bonding. The isoelectric point (iep) of endotoxin is approximately 2. An electrostatic attractive force will be present with aluminum hydroxide adjuvant (iep=11.4), and an electrostatic repulsive force will operate with aluminum phosphate adjuvant (iep=4.6). Endotoxin contains two phosphate groups in the lipid A portion. Covalent bonding occurs with surface aluminum in aluminum hydroxide adjuvant but is inhibited by surface phosphate in aluminum phosphate adjuvant. In-vitro desorption experiments using components of interstitial fluid showed that endotoxin adsorbed by aluminum hydroxide adjuvant was not desorbed by interstitial anions (5 mM phosphate or 2.7 mM citrate) or interstitial proteins (25 mg albumin/ml). The effect of aluminum-containing adjuvants on the systemic response of Sprague-Dawley rats to a 15 microg/kg subcutaneous dose of endotoxin was determined by measuring the serum concentration of tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6). TNF-alpha and IL-6 were observed in the group which received an endotoxin solution or endotoxin and aluminum phosphate adjuvant. No TNF-alpha or IL-6 was detected in the group that received endotoxin and aluminum hydroxide adjuvant . Aluminum hydroxide adjuvant detoxifies endotoxin by adsorbing it in the vaccine and then not releasing it in interstitial fluid upon administration.

Record Date Created: 20010222

50/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10938432 20499050 PMID: 11044072

Efficacy and safety studies of a recombinant chimeric respiratory syncytial virus FG glycoprotein vaccine in cotton rats.

Prince G A; Capiau C; Deschamps M; Fabry L; Garcon N ; Gheysen D; Prieels J P; Thiry G; Van Opstal O; Porter D D

Virion Systems, Inc., Rockville, Maryland 20850, USA. gprince@erols.com

Journal of virology (UNITED STATES) Nov 2000, 74 (22) p10287-92, ISSN 0022-538X Journal Code: 0113724

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Several formulations of a recombinant chimeric respiratory syncytial virus (RSV) vaccine consisting of the extramembrane domains of the F and G glycoproteins (FG) were tested in cotton rats to evaluate efficacy and safety. The FG vaccine was highly immunogenic, providing nearly complete resistance to pulmonary infection at doses as low as 25 ng in spite of inducing relatively low levels of serum neutralizing antibody at low vaccine doses. Upon RSV challenge animals primed with FG vaccine showed quite mild alveolitis and interstitial pneumonitis, which were eliminated by the addition of monophosphoryl lipid A to the formulation.

Record Date Created: 20001121

50/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10649273 20182109 PMID: 10715523
A hepatitis B vaccine formulated with a novel adjuvant system.
Ambrosch F; Wiedermann G; Kundi M; Leroux-Roels G; Desombere I; Garcon N ; Thiriart C; Slaoui M; Thoelen S
Institute for Specific Prophylaxis and Tropical Medicine, University of Vienna, Kinderspitalgasse 15, A-1095, Wien, Austria.
Vaccine (ENGLAND) Apr 14 2000, 18 (20) p2095-101, ISSN 0264-410X Journal Code: 8406899
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Although more than 95% of the vaccinated population responds to the currently licensed vaccines against hepatitis B, some groups were found to be low responders. Lipid A as adjuvant, through its ability to activate macrophages, might improve humoral as well as cellular immune response. Therefore we evaluated the profile of a hepatitis B vaccine with the new adjuvant system SBAS4. 150 young adults were enrolled and randomized into three groups: one received the SBAS4 hepatitis B vaccine, the second Engerix-B(TM) and the third a hepatitis B vaccine with an alternative formulation on alum. Vaccinations were at 0 and 6 months. The vaccine was well tolerated. At month 7 all vaccinees were protected but with significant differences in GMTs between groups: 13,271 mIU/ml for the SBAS4 group versus 1203 and 1823 mIU/ml. Hence the hepatitis B vaccine with the new adjuvant system is more immunogenic compared to the other vaccines containing the same antigen and could be suitable for a two dose schedule.
Record Date Created: 20000711

50/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10322626 99308797 PMID: 10381090
Purification and characterization of hepatitis B virus surface antigen particles produced in Drosophila Schneider-2 cells.
Deml L; Schirmbeck R; Reimann J; Wolf H; Wagner R
Institute of Medical Microbiology, Klinikum Regensburg, University of Regensburg, Germany.
Journal of virological methods (NETHERLANDS) May 1999, 79 (2) p205-17, ISSN 0166-0934 Journal Code: 8005839
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The small surface antigen of hepatitis B virus (HBV) was produced in Drosophila melanogaster Schneider-2 (DS-2) cells transfected stably using an inducible Drosophila metallothionein promoter. Selected clonal DS-2 cell-lines expressed and secreted large quantities of HBsAg particles consisting exclusively of non-glycosylated 25 kDa proteins. HBsAg produced by DS-2 cells had physical and biochemical properties very similar to 22 nm particles derived from the human hepatoma cell-line PLC/PRF/5. DS-2 cell-derived HBsAg particles were purified near homogeneity by a strategy based on protein concentration, precipitation and ultracentrifugation. The resulting HBsAg product was < 98% pure. A single immunisation of BALB/c mice with both DS-2 and yeast-cell derived purified HBsAg particles without adjuvants elicited a substantial humoral antibody and class-I

restricted cytotoxic T lymphocyte (CTL) response. Adsorption of HBsAg particles to aluminium hydroxide resulted in increased levels of HBsAg-specific antibodies. However, CTLs were not elicited by HBsAg/Alum combinations. Thus, stably transfected DS-2 cells provide a useful source for the production of HBV subviral particles for diagnostic and research purposes as well as for novel vaccine development.
Record Date Created: 19990810

50/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10230003 99210744 PMID: 10194840
Adjuvant activity of immunopotentiating reconstituted influenza virosomes (IRIVs).
Gluck R
Swiss Serum & Vaccine Institute Berne, Switzerland. r.glueck@-bluewin.ch
Vaccine (ENGLAND) Mar 26 1999, 17 (13-14) p1782-7, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Using immunopotentiating, reconstituted influenza virosomes (IRIV) as a delivery vehicle, a number of vaccines have been developed. In humans, IRIV-based vaccines containing hepatitis A and influenza antigens have been found to possess enhanced immunogenicity compared to alum - adsorbed vaccine for hepatitis A or commercial subunits or whole virion influenza vaccines. These vaccines were safe and did not engender any antiphospholipid antibodies against the liposome components of the IRIV. Hepatitis B , tetanus toxoid and diphtheria toxoid, and nucleic acids have also been incorporated into IRIVs. These vaccines are now undergoing clinical phase I testing. IRIVs are also being evaluated in phase I trials for their ability to deliver antigens by the intranasal route.
Record Date Created: 19990527

50/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10050478 99012148 PMID: 9796056
Enhanced immunogenicity of a recombinant genital warts vaccine adjuvanted with monophosphoryl lipid A .
Thompson H S; Davies M L; Watts M J; Mann A E; Holding F P; O'Neill T; Beech J T; Thompson S J; Leesman G D; Ulrich J T
Cantab Pharmaceuticals Research Ltd, Cambridge, UK.
Vaccine (ENGLAND) Dec 1998, 16 (20) p1993-9, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The regression of genital warts is believed to be a T-cell-mediated immune effect. We have sought to enhance the immunogenicity of a therapeutic vaccine for the treatment of genital warts with the use of the adjuvant monophosphoryl lipid A (MPL-immunostimulant), a detoxified form of the lipopolysaccharide (LPS) of Salmonella minnesota R595. The

comparative immunogenicity and reactogenicity of a recombinant human papillomavirus type 6 (HPV6) L2E7 fusion protein in either aqueous, oil-in-water emulsions or Alhydrogel formulations containing MPL was evaluated. We conclude that the simple addition of MPL to the L2E7 fusion protein already adsorbed onto Alhydrogel preferentially enhances antigen specific in vitro T-cell proliferative responses, IFN gamma production and in vivo delayed type hypersensitivity responses without increasing its reactogenicity.
Record Date Created: 19981231

50/7/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10035090 99022993 PMID: 9806046
Long-term efficacy and immune responses following immunization with the RTS,S malaria vaccine.
Stoute J A; Kester K E; Krzych U; Wellde B T; Hall T; White K; Glenn G; Ockenhouse C F; Garcon N ; Schwenk R; Lanar D E; Sun P; Momin P; Wirtz R A ; Golenda C; Slaoui M; Wortmann G; Holland C; Dowler M; Cohen J; Ballou W R
Department of Immunology, Walter Reed Army Institute of Research, Washington, DC, USA. stoutej@wrsmtp-ccmail.army.mil
Journal of infectious diseases (UNITED STATES) Oct 1998, 178 (4) p1139-44, ISSN 0022-1899 Journal Code: 0413675
Document type: Clinical Trial; Controlled Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The malaria sporozoite vaccine candidate RTS,S, formulated with an oil-in-water emulsion plus the immunostimulants monophosphoryl lipid A and the saponin derivative QS21 (vaccine 3), recently showed superior efficacy over two other experimental formulations. Immunized volunteers were followed to determine the duration of protective immune responses. Antibody levels decreased to between one-third and one-half of peak values 6 months after the last dose of vaccine. T cell proliferation and interferon-gamma production in vitro were observed in response to RTS,S or hepatitis B surface antigen. Seven previously protected volunteers received sporozoite challenge, and 2 remained protected (1/1 for vaccine 1, 0/1 for vaccine 2, and 1/5 for vaccine 3). The prepatent period was 10.8 days for the control group and 13.2 days for the vaccinees ($P < .01$). Immune responses did not correlate with protection. Further optimization in vaccine composition and/or immunization schedule will be required to induce longer-lasting protective immunity.
Record Date Created: 19981120

50/7/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09833053 98261539 PMID: 9596760
Liposomes containing lipid A serve as an adjuvant for induction of antibody and cytotoxic T-cell responses against RTS,S malaria antigen.
Richards R L; Rao M; Wassef N M; Glenn G M; Rothwell S W; Alving C R
Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Washington, D.C. 20307-5100, USA. dr. roberta owens@wrsmtp-ccmail.army.mil
Infection and immunity (UNITED STATES) Jun 1998, 66 (6) p2859-65,

ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Encapsulation of soluble protein antigens in liposomes was previously shown to result in processing of antigen via the major histocompatibility complex class I pathway, as evidenced by costaining of the trans-Golgi region of murine bone marrow-derived macrophages (BMs) by fluorophore-labeled liposomal antigen and by a trans-Golgi-specific fluorescent lipid. Evidence is presented here that free or liposome-encapsulated RTS,S, a particulate malaria antigen consisting of hepatitis B particles coexpressed with epitopes from the Plasmodium falciparum circumsporozoite protein, also was localized in the trans-Golgi after incubation with BMs, suggesting processing by the class I pathway. An in vivo cytotoxic T-lymphocyte (CTL) response was detected, however, only after immunization with RTS,S encapsulated in liposomes containing lipid A and not after immunization with free RTS,S or with RTS,S encapsulated in liposomes lacking lipid A. Therefore, intracellular delivery of antigen containing CTL epitopes to the Golgi of BMs does not necessarily result in a CTL response in vivo unless an additional adjuvant, such as liposomes containing lipid A, is utilized. Encapsulation of RTS,S in liposomes containing monophosphoryl lipid A (MPL) resulted in a dose-dependent enhancement of the NANP-specific immunoglobulin G (IgG) antibody response compared to that of free RTS,S. The IgG1 and IgG2a subclasses predominated after immunization with RTS,S encapsulated in liposomes containing MPL. These results demonstrate that encapsulation of a lipid-containing particulate antigen, such as RTS, S, in liposomes containing lipid A can enhance both humoral and cellular immune responses.

Record Date Created: 19980625

50/7/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09235367 97120469 PMID: 8961140

Liposomal subunit vaccines: effects of lipid A and aluminum hydroxide on immunogenicity.

Richards R L; Alving C R; Wassef N M

Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Washington, DC 20307-5100, USA.

Journal of pharmaceutical sciences (UNITED STATES) Dec 1996, 85 (12) p1286-9, ISSN 0022-3549 Journal Code: 2985195R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Protein and peptide antigens frequently are only slightly immunogenic when utilized alone in vaccines. Formulation of these antigens in a carrier vehicle, particularly when an adjuvant is included, often results in markedly enhanced immune responses. Encapsulation of peptide and protein antigens in liposomes generally results in a relatively slight enhancement of antibody production compared with that observed with the antigen alone. However, when lipid A is included in the liposomes, immunogenicity is markedly increased compared both with antigen alone and with antigen encapsulated in liposomes lacking lipid A . The enhancement of the immune response caused by lipid A is dependent on the liposomal lipid

A dose. Aluminum salts, such as aluminum hydroxide and aluminum phosphate, act as adjuvants for some antigens and are used in a variety of human vaccines. When liposomes containing encapsulated protein or peptide antigens were adsorbed with aluminum hydroxide , an enhancement of the antibody response was observed with some antigens, whereas with other antigens the presence of aluminum hydroxide either had no effect or resulted in a diminished antibody response. Immunogenicity of protein and peptide antigens can be enhanced by formulation in liposomes containing lipid A and, depending on the antigen , can be enhanced further by adsorption of the liposomal antigen formulation with aluminum salts.
Record Date Created: 19970306

50/7/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09174595 97078136 PMID: 8920703
Adjuvant properties of non-phospholipid liposomes (Novasomes) in experimental animals for human vaccine antigens.
Gupta R K; Varanelli C L; Griffin P; Wallach D F; Siber G R
Massachusetts Public Health Biologic Laboratories, State Laboratory Institute, Boston 02130, USA.
Vaccine (ENGLAND) Feb 1996, 14 (3) p219-25, ISSN 0264-410X
Journal Code: 8406899
Contract/Grant No.: AI33575; AI; NIAID
Erratum in Vaccine 1996 Jun;14(8) 1
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Non-phospholipid liposomes composed of dioxyethylene cetyl ether, cholesterol and oleic acid were evaluated as adjuvants with human vaccine antigens, tetanus toxoid (TT) and diphtheria toxoid (DT), in mice and rabbits. Antigens encapsulated in or mixed with liposomes elicited antitoxin levels similar to those elicited by antigens given with Freund's adjuvant or adsorbed onto aluminum phosphate . All liposomal antigen preparations, antigen given with Freund's adjuvant or adsorbed onto aluminum phosphate , elicited significantly higher IgG antibodies and antitoxin levels than soluble antigens in mice after a single injection and in rabbits after each of three injections. TT encapsulated in liposomes elicited sustained anti-TT IgG antibody levels in mice after a single injection as compared to TT mixed with liposomes. TT mixed with or encapsulated within liposomes containing monophosphoryl lipid A /squalene or squalene alone, as well as aluminum phosphate adsorbed TT elicited greater primary responses in mice than TT mixed with or encapsulated within plain liposomes. Liposomal TT preparations produced a slightly higher anamnestic response in mice than aluminum phosphate adsorbed TT. Subclass analysis of anti-TT antibodies showed that the majority of the antibodies belong to IgG1 subclass. Liposomal TT preparations, particularly those with encapsulated monophosphoryl lipid A /squalene or squalene alone, consistently elicited higher levels of anti-TT IgG2a and IgG2b than aluminum phosphate adsorbed or soluble TT. None of the preparations elicited IgG3 or IgM antibodies. It appears that non-phospholipid liposomes are as potent adjuvants as the currently employed adjuvant for human vaccines (aluminum phosphate) or a benchmark adjuvant for experimental immunology (Freund's adjuvant), and may be able to modulate the immune response towards the Th1 type.

Record Date Created: 19970114

50/7/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09123717 97006736 PMID: 8854029
Mimicry of viral epitopes with retro-inverso peptides of increased stability.
Benkirane N; Guichard G; Briand J P; Muller S; Brown F; Van Regenmortel M H
Institut de Biologie Moleculaire et Cellulaire, CNRS, Strasbourg, France.
Developments in biological standardization (SWITZERLAND) 1996, 87 p283-91, ISSN 0301-5149 Journal Code: 0427140
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Two major limitations to the use of peptides as synthetic vaccines are their poor immunogenicity and low antigenic cross-reactivity with the epitopes of virus particles . Recently it has been shown that retro-inverso peptides corresponding to an immunodominant epitope of foot-and-mouth disease virus (FMDV) are able to mimic the structure and antigenic activity of natural L-peptides [1]. A series of L- and retro-inverso peptides of the loop 141-159 of the VP1 protein of FMDV has been synthesized. Antibodies to these peptides were produced by injecting rabbits with peptides covalently coupled to small unilamellar liposomes containing monophosphoryl lipid A as adjuvant. The retro-inverso peptides led to higher serum antibody titres which appeared earlier after the start of immunization and lasted longer than those found with L-peptides. Antibodies to retro-inverso peptides cross-reacted strongly with L-peptides and with virus particles , while guinea pig antisera to VP1 protein and virions cross-reacted strongly with the retro-inverso peptides. In view of their increased stability compared to natural L-peptides, retro-inverso peptidomimetics have considerable potential as synthetic viral vaccines.
Record Date Created: 19970210

50/7/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08998221 96351459 PMID: 8717391
Hybrid hepatitis B virus core antigen as a vaccine carrier moiety: I. presentation of foreign epitopes.
Schodel F; Peterson D; Hughes J; Wirtz R; Milich D
INSERM U 80, Hopital Edouard Herriot, Lyon, France.
Journal of biotechnology (NETHERLANDS) Jan 26 1996, 44 (1-3) p91-6, ISSN 0168-1656 Journal Code: 8411927
Contract/Grant No.: AI20720; AI; NIAID; AI33562; AI; NIAID
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis B virus (HBV) core antigen (HBcAg) is a highly immunogenic subviral particle. Here, we review recent progress in the use of HBcAg as a carrier moiety for heterologous epitopes. To define surface exposed and

immunogenic insertion sites for foreign epitopes in HBcAg, peptidic epitopes representing binding sites for virus neutralizing antibodies on the HBV surface antigens were inserted at different positions within HBcAg using genetic engineering in an Escherichia coli expression system (Schodel et al. (1992) J. Virol. 66, 106-114). While fusion to the N-terminus required a linker to become surface accessible, both fusion to the N-terminus and to the C-terminus was compatible with particle assembly and preserved the native antigenicity and immunogenicity of HBcAg. Fusion to an immunodominant internal site of HBcAg reduced the HBcAg immunogenicity and antigenicity and most drastically enhanced the immunogenicity of the inserted foreign epitope. This internal site of HBcAg was used to express circumsporozoite antigen (CS) repeat epitopes of two rodent malaria parasites and of Plasmodium falciparum (Schodel et al. (1994b) J. Exp. Med. 180, 1037-1046 and Schodel et al. (1995a) 95th ASM General Meeting, Washington DC, Abstr. E61). When purified from recombinant Salmonella typhimurium, the hybrid HBcAg-CS proteins were particulate and displayed CS antigenicity as well as reduced HBc antigenicity, as compared to native HBcAg. Immunization of several mouse strains with HBcAg-CS hybrid particles resulted in high titered serum anti-CS antibodies representing all murine IgG isotypes. Immunization of mice with HBcAg or HBcAg-CS particles formulated on alum , complete Freunds or incomplete Freunds adjuvant resulted in equivalent anti-CS and anti-HBc serum antibody titres. The possible influence of carrier-specific immunosuppression was examined and pre-existing immunity to HBcAg did not significantly alter the immunogenicity of hybrid HBcAg particles suggesting that they would be useful carrier moieties for repeated immunizations against multiple haptens or in immune subjects after HBV infection. Examination of T cell recognition of HBcAg-CS particles revealed that HBcAg-specific T cells were universally primed and CS-specific T cells were primed if the insert contained a CS-specific T cell recognition site. This indicates that the internal amino acid position in HBcAg is permissive for the inclusion of heterologous functional T helper as well as B cell epitopes. BALB/c mice immunized with HBcAg-CS1 were protected against P. berghei challenge to 90% and 100%, respectively, in two independent experiments. (14 Refs.)
Record Date Created: 19961016

50/7/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08787025 96125906 PMID: 8573840
Development of cationically modified cellulose adsorbents for the removal of endotoxins.
Weber C; Henne B; Loth F; Schoenhofen M; Falkenhagen D
Institute of Bioengineering, Science Academy of Lower Austria, Krems, Austria.
ASAIO journal (American Society for Artificial Internal Organs : 1992) (UNITED STATES) Jul-Sep 1995, 41 (3) pM430-4, ISSN 1058-2916
Journal Code: 9204109
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The removal of endotoxins by extracorporeal adsorption processes seems the most promising therapeutic approach to Gram-negative sepsis and endotoxin shock. However, thus far adsorbents have failed to bind endotoxins efficiently or have shown adverse biocompatibility

characteristics. To overcome these disadvantages, small particles of regenerated cellulose in the range of 1-8 microns in diameter were produced. Before use, the microspheres were cationically modified by substitution with polyethyleneimine (PEI) or diethylaminoethyl (DEAE) groups. A third kind of adsorbent was manufactured by (physically) coating the cellulose matrix with PEI. All three types of adsorbents exhibited a high adsorption capacity for endotoxins in human plasma, whereas activated charcoal and various anion exchange resins removed only small amounts of endotoxins under the same conditions. In addition, because the outer surface area is very large, adsorption takes place rapidly and diffusion becomes almost irrelevant. The adsorption process is primarily based on electrostatic interactions, which could be demonstrated by a significantly higher adsorption rate and binding capacity for lipid A -diphosphoryl, compared with lipid A - monophosphoryl . Use of these adsorbents in a newly developed plasma sorption system could be of great clinical interest because of the low production costs, the high adsorption efficiency, and the excellent biocompatibility data.
Record Date Created: 19960312

50/7/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08741964 96100700 PMID: 7590830
Liposomes as carriers of peptide antigens: induction of antibodies and cytotoxic T lymphocytes to conjugated and unconjugated peptides.
Alving C R; Koulchin V; Glenn G M; Rao M
Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Washington, DC 20307-5100, USA.
Immunological reviews (DENMARK) Jun 1995, 145 p5-31, ISSN 0105-2896 Journal Code: 7702118
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In the quest for effective immunization against complex diseases such as cancer, parasitic diseases, AIDS, and other viral infections, numerous peptides and recombinant proteins have been synthesized, examined for the ability to induce antibodies and CTLs, and tested for binding capability and therapeutic or prophylactic efficacy against the original target cell or organism. A liposome formulation, consisting of alum - adsorbed liposomes containing both a potent adjuvant , lipid A , and encapsulated or surface bound antigen, has had a record of safety and strong effectiveness for induction of antibodies in human vaccine trials. These same liposomes can also serve as effective vehicles for delivering conjugated or unconjugated peptides and proteins to antigen presenting cells for presentation via MHC class I and class II pathways for induction of CTLs and antibodies in experimental animal models. Liposomal lipid A appears to be extremely important, and is often a requirement, as an adjuvant for induction of CTLs against liposomal peptide antigens. Computer-generated molecular modelling analysis of small unconjugated or lipid-conjugated peptides strongly suggests that the expression of peptide antigen on the surface of the liposomes can be an important factor both in the induction of antibodies and in determining antibody specificities to small peptides. However, antigenic surface expression of liposomal peptide is not required for induction of CTLs. The data suggest that small synthetic peptides, synthesized with or without a lipid tail, or chemically

conjugated to the surface of liposomes, might serve as effective antigenic epitopes, in combination with liposomal lipid A for induction of antibodies and CTLs. (104 Refs.)
Record Date Created: 19951226

50/7/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08526644 95282495 PMID: 7762283
Effects of muramyl dipeptide derivatives as adjuvants on the induction of antibody response to recombinant hepatitis B surface antigen.
Tamura M; Yoo Y C; Yoshimatsu K; Yoshida R; Oka T; Ohkuma K; Arikawa J; Azuma I
Institute of Immunological Science, Hokkaido University, Sapporo, Japan.
Vaccine (ENGLAND) Jan 1995, 13 (1) p77-82, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The ability of two muramyl dipeptide (MDP) derivatives, B30-MDP and MDP-Lys(L18), to enhance the immunogenicity of recombinant hepatitis B surface antigen (rHBsAg) was examined. When mice were immunized intraperitoneally with rHBsAg together with each MDP derivative, the antibody titres were higher than those in mice immunized with alum - adsorbed rHBsAg, which is a commercially available hepatitis B vaccine. When mice were given a subcutaneous or intramuscular injection of rHBsAg and either MDP derivative, the antibody titres were the same as those in mice given alum - adsorbed rHBsAg. These results indicate the usefulness of MDP derivatives as immunoadjuvants for a new-generation vaccine.
Record Date Created: 19950628

50/7/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08206965 94342820 PMID: 7520465
Immunity to malaria elicited by hybrid hepatitis B virus core particles carrying circumsporozoite protein epitopes.
Schodel F; Wirtz R; Peterson D; Hughes J; Warren R; Sadoff J; Milich D
Department of Bacterial Diseases, Walter Reed Army Institute of Research, Washington, DC 20307-5100.
Journal of experimental medicine (UNITED STATES) Sep 1 1994, 180 (3) p1037-46, ISSN 0022-1007 Journal Code: 2985109R
Contract/Grant No.: AI-20720; AI; NIAID; AI-33562; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The hepatitis B virus (HBV) nucleocapsid antigen (HBcAg) was investigated as a carrier moiety for the immunodominant circumsporozoite (CS) protein repeat epitopes of Plasmodium falciparum and the rodent malaria agent P. berghei. For this purpose hybrid genes coding for [NANP]4 (C75CS2) or [DP4NPN]2 (C75CS1) as internal inserts in HBcAg (between amino acids 75 and 81) were constructed and expressed in recombinant Salmonella

typhimurium. The resulting hybrid HBcAg-CS polypeptides purified from S. typhimurium were particulate and displayed CS and HBc antigenicity, however, the HBc antigenicity was reduced compared to native recombinant HBcAg. Immunization of several mouse strains with HBcAg-CS1 and HBcAg-CS2 particles resulted in high titer, P.berghei- or P.falciparum-specific anti-CS antibodies representing all murine immunoglobulin G isotypes. The possible influence of carrier-specific immunosuppression was examined, and preexisting immunity to HBcAg did not significantly affect the immunogenicity of the CS epitopes within HBcAg-CS1 particles . Similarly, the choice of adjuvant did not significantly alter the immunogenicity of HBcAg-CS hybrid particles. Immunization in complete or incomplete Freund's adjuvant or alum resulted in equivalent anti-HBc and anti-CS humoral responses. Examination of T cell recognition of HBcAg-CS particles revealed that HBcAg-specific T cells were universally primed and CS-specific T cells were primed if the insert contained a CS-specific T cell recognition site. This indicates that the internal site in HBcAg is permissive for the inclusion of heterologous pathogen-specific T as well as B cell epitopes. Most importantly, 90 and 100% of BALB/c mice immunized with HBcAg-CS1 particles were protected against a P. berghei challenge infection in two independent experiments. Therefore, hybrid HBcAg-CS particles may represent a useful approach for future malaria vaccine development.
Record Date Created: 19940922

50/7/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08026403 94149828 PMID: 8107205
Antibody and cytotoxic T-cell responses to soluble hepatitis B virus (HBV) S antigen in mice: implication for the pathogenesis of HBV-induced hepatitis.
Schirmbeck R; Melber K; Mertens T; Reimann J
Department of Bacteriology, University of Ulm, Germany.
Journal of virology (UNITED STATES) Mar 1994, 68 (3) p1418-25, ISSN 0022-538X Journal Code: 0113724
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Immune responses to components of hepatitis B virus (HBV) are assumed to play an essential role not only in the elimination of the virus but also in the pathogenesis of HBV-induced hepatitis. Protective humoral immunity to HBV is mediated by immune responses to HBV surface antigen (HBsAg). It is important to know which HBsAg preparations induce which type of cellular and humoral immune responses under which immunization conditions. We studied in BALB/c mice the humoral (antibody) response and the class I-restricted cytotoxic T-lymphocyte (CTL) response to different preparations of HBsAg particles: recombinant, small protein particles; plasma-derived, mixed particles formed by large, medium, and small surface proteins; and different preparations of recombinant, mixed particles formed by large and small surface proteins. Specific antibody levels appeared in the sera of immunized mice 2 to 3 weeks after immunization and were correlated with the antigen dose used for priming. HBsAg-specific antibody levels were enhanced by boost injections or by adsorbing the antigen to aluminum hydroxide . Injected in particulate form without adjuvants in the dose range of 0.1 to 10 micrograms per mouse, all HBsAg preparations tested efficiently primed specific CD8+ CTL of defined restriction and

epitope specificity. Specific CTL reactivity was detectable from 5 days to more than 4 months postimmunization. In the dose range tested, it was independent of the antigen dose used for immunization and not enhanced by repeated boost injections. CTL were not elicited by HBsAg adsorbed to aluminum hydroxide . We have thus defined conditions under which HBsAg induced preferentially either a cellular immune response or a humoral immune response. These findings may be relevant for the interpretation of HBV-associated immunopathologic phenomena.
Record Date Created: 19940323

50/7/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07886029 94025163 PMID: 8212222
Characterization and administration of cyclosporine liposomes as a small-particle aerosol.
Gilbert B E; Wilson S Z; Garcon N M ; Wyde P R; Knight V
Department of Microbiology and Immunology, Baylor College of Medicine, Houston, Texas 77030.
Transplantation (UNITED STATES) Oct 1993, 56 (4) p974-7, ISSN 0041-1337 Journal Code: 0132144
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Systemically administered CsA has not consistently suppressed the pulmonary immunoreactivity that leads to rejection in lung transplant patients. Pulmonary T cells from patients given CsA systemically still retain their immunoreactivity, which can be suppressed with added CsA. Direct application of CsA by aerosol to the respiratory epithelium should achieve high lung concentrations with minimum systemic effects. In the present study, CsA was most efficiently incorporated into liposomes composed of egg yolk phosphatidylcholine at a molar ratio of CsA to egg yolk phosphatidylcholine of 1:20. These CsA liposomes retained their biological activity and were as effective as free CsA in the suppression of anti-CD3-stimulated [3H]thymidine incorporation by mouse spleen cells. The generation of a small- particle aerosol of CsA liposomes had no effect on this biological activity. CsA liposome aerosol particles have a mass median aerodynamic diameter of 2 microns, which allows for distribution of drug throughout the respiratory tract. Quantitation of CsA in the lungs and blood of mice exposed to CsA liposome aerosols for 4 days showed that as little as 15 min daily (0.11 mg/kg/day) was sufficient to achieve an estimated concentration of CsA in respiratory secretions of 6 micrograms/ml without detectable blood levels. Thus, CsA liposomes can be produced and aerosolized that achieve pulmonary concentrations with sufficient immunosuppressive activity to be effective in the treatment of lung diseases.
Record Date Created: 19931119

50/7/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07716121 93237302 PMID: 8476912
Coupling of ligands to liposomes independently of solute entrapment: observations on the formed vesicles.

Gregoriadis G; Garcon N ; da Silva H; Sternberg B
Centre for Drug Delivery Research, School of Pharmacy, London, UK.
Biochimica et biophysica acta (NETHERLANDS) Apr 22 1993, 1147 (2) p185-93, ISSN 0006-3002 Journal Code: 0217513
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Bovine serum albumin (BSA), employed as a model ligand, was covalently linked (about 16% of the amount used) to small unilamellar vesicles (SUV) composed of phospholipid, cholesterol and N-(p-aminophenyl)stearylamide (APSA) (molar ratios 1:1:0.05). SUV with bound BSA were then used to generate dehydration-rehydration vesicles (DRV) in the presence of tetanus toxoid and/or carboxyfluorescein (CF). Nearly all of the SUV-bound BSA (about 15% of the original amount) was recovered in the multilamellar DRV formed, with a considerable proportion (42-62%) of the ligand becoming available on the outer bilayers. This apparent spatial reorientation of BSA within DRV also caused the entrapped toxoid to shift to some extent to the liposomal surface. There was no significant difference in the z average mean size between DRV with and without coupled BSA (543 and 555 nm diameter, respectively). Percent number diameter distribution data revealed that 71.2 (BSA-free) and 76.4% (BSA-containing DRV) of the vesicles had diameters of about 300-440 and 330-420 nm, respectively. However, in terms of percent mass diameter distribution, 69.5% (BSA-free) and 65.2% (BSA-containing DRV) of the mass was in vesicles with corresponding ranges of diameter of 1381-2975 and 1086-2840 nm. Vesicle size heterogeneity in both preparations was confirmed by freeze-fracture electron microscopy which also indicated that structures with or without bound BSA, were mostly vesicular of the multilamellar type. Judging from CF latency values, ligand-bearing DRV were stable on incubation with blood plasma at 37 degrees C for 24 h. Stability was, however, reduced significantly when the amount of ligand bound was excessive. The present approach allows for the coupling of ligands to and the entrapment of antigens and other labile solutes in liposomes independently, thus avoiding potential damage of such solutes by the coupling reagents.

Record Date Created: 19930524

50/7/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07582361 93110957 PMID: 1471412
Immunopotentiating reconstituted influenza virosomes (IRIVs) and other adjuvants for improved presentation of small antigens.
Gluck R
Department of Virology, Swiss Serum and Vaccine Institute, Berne.
Vaccine (ENGLAND) 1992, 10 (13) p915-9, ISSN 0264-410X Journal Code: 8406899
Document type: Clinical Trial; Clinical Trial, Phase I; Clinical Trial, Phase II; Controlled Clinical Trial; Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Synthetic peptides, purified subunits or inactivated small virus particles require immunopotentiation if they are to be effective vaccines. A large range of procedures to enhance immunogenicity has evolved over the

last decades: aluminium salts, proteosomes, immunostimulating complexes (ISCOMs), liposomes, conjugation with bacterial products or derivatives, combination with surface-active agents or application of cytokines have been the most described classes of adjuvants. We describe here the design of an inactivated hepatitis A vaccine adjuvanted with immunopotentiating reconstituted influenza virosomes (IRIVs). The formalin-inactivated hepatitis A particles are attached to reconstituted protein-lipid complexes consisting of a mixture of phospholipids and influenza virus glycoproteins. With this new vaccine design we combined different immunostimulating effects: immunopotentiation by phospholipid vesicles, recognition of the haemagglutinin (HA) epitopes by the immune system, binding capacity of HA to sialic acid-containing receptors of macrophages and immunocompetent cells and mediation of entry into the cytoplasm of macrophages by a membrane-fusion event triggered by HA. Hepatitis A seronegative human volunteers received one intramuscular injection with this new vaccine. There were only few mild local reactions and 14 days after vaccination 100% of the subjects were seropositive. Among the individuals (control group) who received an alum - adsorbed vaccine, 88% developed local reactions. The seroconversion rate was 44%. We conclude from these results that the IRIVs provide a new approach to the future design of adjuvanted vaccines. (19 Refs.)
Record Date Created: 19930122

50/7/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07533812 93058206 PMID: 1331390
Evaluation of biodegradable microspheres as vaccine adjuvant for hepatitis B surface antigen.
Nellore R V; Pande P G; Young D; Bhagat H R
Department of Pharmaceutics, School of Pharmacy, University of Maryland, Baltimore.
Journal of parenteral science and technology : a publication of the Parenteral Drug Association (UNITED STATES) Sep-Oct 1992, 46 (5) p176-80, ISSN 0279-7976 Journal Code: 8103145
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Biodegradable microspheres were evaluated as vaccine adjuvants based on their ability to provide prolonged release of incorporated agents. Hepatitis B surface antigen (HBSA) prepared by recombinant DNA technology was chosen as a model antigen and encapsulated into polyglycolic acid (PGA) by solvent extraction and solvent evaporation techniques. Five microsphere formulations were prepared to evaluate effect of microsphere size and the presence of immunostimulants such as muramyl dipeptide (MDP) or aluminum hydroxide. The microspheres were characterized for size distribution, surface morphology and antigenicity. Guinea pigs were chosen as the animal model for evaluation of antigenicity of the formulations. The animals were divided into seven groups of four animals each and the microsphere formulations were injected intraperitoneally, using alum adsorbed HBSA as positive control and placebo microspheres as negative control. Blood samples were withdrawn from the animals by toe clipping at two, four, six and sixteen weeks and plasma was analyzed for antibodies against hepatitis B by an enzyme linked immunoassay. At sixteen weeks, the animals were reinjected and evaluated for antibody response at two,

four and six weeks post second injection. Antibody response to the microspheres was higher than control. Smaller size microspheres elicited earlier antibody response while the larger size microspheres provided delayed and longer duration of antibody production. Microspheres with MDP potentiated the antibody response. The results demonstrate the applicability of biodegradable microspheres for immunization against hepatitis B .
Record Date Created: 19921222

50/7/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07192337 92108054 PMID: 1729706
Liposomal malaria vaccine in humans: a safe and potent adjuvant strategy.
Fries L F; Gordon D M; Richards R L; Egan J E; Hollingdale M R; Gross M; Silverman C; Alving C R
Center for Immunization Research, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, MD 21205.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jan 1 1992, 89 (1) p358-62, ISSN 0027-8424 Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
This study describes the safety and immunogenicity of a liposome-based vaccine injected into human subjects. Thirty healthy adult male volunteers were immunized with a liposome-encapsulated recombinant protein (R32NS181) containing epitopes from the repeat region of the circumsporozoite protein of Plasmodium falciparum. This antigen had previously been found to be poorly immunogenic in humans when it was adsorbed with Al(OH)3. In the present study, R32NS181 was encapsulated in liposomes containing monophosphoryl lipid A that were subsequently adsorbed to Al(OH)3. Increasing doses of liposomes containing antigen and monophosphoryl lipid A were used, but the liposomes were always adsorbed to the same dose of Al(OH)3. R32-specific serum IgG antibody responses to liposome-encapsulated R32NS181 were much higher than levels attained previously in humans with R32NS181 adsorbed to Al(OH)3. Geometric mean specific IgG levels after three doses ranged from 14 to 33 micrograms/ml. Sera from volunteers receiving the two highest doses inhibited P. falciparum sporozoite invasion of cultured hepatoma cells by an average of 92%, a result that was again superior to previously reported vaccines. Moderate but acceptable transient local reactogenicity was noted at high doses of the vaccine formulation, but little or no systemic toxicity was seen despite liposomal monophosphoryl lipid A doses up to 2200 micrograms. We conclude that encapsulation of poorly immunogenic circumsporozoite protein repeat peptides in monophosphoryl lipid A -containing liposomes is a successful adjuvant strategy in humans for inducing high levels of specific antibody production.
Record Date Created: 19920212

50/7/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07105401 92040138 PMID: 1937803

Preparation, characterization, and immunogenicity of conjugates composed of the O-specific polysaccharide of Shigella dysenteriae type 1 (Shiga's bacillus) bound to tetanus toxoid.

Chu C Y; Liu B K; Watson D; Szu S S; Bryla D; Shiloach J; Schneerson R; Robbins J B

Laboratory of Developmental and Molecular Immunity, National Institute of Child Health and Human Development, Bethesda, Maryland 20892.

Infection and immunity (UNITED STATES) Dec 1991, 59 (12) p4450-8, ISSN 0019-9567 Journal Code: 0246127

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The background for developing conjugate vaccines for shigellosis composed of the O-specific polysaccharide (O-SP) bound to a protein is described elsewhere (C. Y. Chu, R. Schneerson, and J. B. Robbins, submitted for publication). Briefly, there is direct evidence for type (lipopolysaccharide [LPS])-specific protection after infection with the wild type or with attenuated strains of shigellae. Prospective studies of Israeli armed forces recruits show a correlation between preexisting serum immunoglobulin G (IgG) LPS antibodies and resistance to shigellosis (D. Cohen, M. S. Green, C. Block, R. Slephon, and I. Ofek, J. Clin. Microbiol. 29:386-389, 1991). In order to elicit IgG LPS-specific antibodies to Shigella dysenteriae type 1, the O-SP of this pathogen was purified and bound to tetanus toxoid (TT) by three schemes. The most immunogenic used a modification of a published method (C. Y. Chu, R. Schneerson, J. B. Robbins, and S. C. Rastogi, Infect. Immun. 40:245-256, 1983). The resultant O-SP-TT conjugates were stable and elicited high levels of IgG O-SP antibodies and booster responses in young mice when injected subcutaneously in saline at 1/10 the proposed human dose. Adsorption onto alum or concurrent administration with monophosphoryl lipid A enhanced both the IgG and IgM antibody responses to the O-SP of the conjugate; both the nonadsorbed and adsorbed conjugates elicited higher rises of IgG than of IgM antibodies. Clinical evaluations of S. dysenteriae type 1 O-SP-TT conjugates are planned.

Record Date Created: 19911224

50/7/28 (Item 28 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06816083 91131152 PMID: 2283158

Liposomes containing lipid A : a potent nontoxic adjuvant for a human malaria sporozoite vaccine.

Alving C R; Richards R L

Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Washington, DC 20307-5100.

Immunology letters (NETHERLANDS) Aug 1990, 25 (1-3) p275-9, ISSN 0165-2478 Journal Code: 7910006

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Liposomes containing lipid A have been developed as adjuvants for inducing humoral immunity to synthetic antigens containing repeat sequence epitopes from the circumsporozoite protein of Plasmodium falciparum. Preclinical studies demonstrated that liposomes containing lipid A and

encapsulated antigen could overcome immunosuppression observed with antigen alone. When liposomes containing lipid A were adsorbed with aluminum hydroxide (alum), further stimulation of humoral immunity against encapsulated antigen was observed in animals. In the presence of huge doses of liposomal lipid A pyrogenicity was not observed and adjuvant activity was enhanced. A phase I human clinical trial has been initiated utilizing a vaccine containing a synthetic recombinant antigen and monophosphoryl lipid A in liposomes and nonliposomal alum as a further adjuvant. Preliminary results confirm that the vaccine lacks significant acute toxicity in humans and causes very strong specific humoral immunity against the appropriate epitopes of the target antigen. (27 Refs.)

Record Date Created: 19910320

50/7/29 (Item 29 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06420681 90118302 PMID: 2692333

Immunogenicity of liposomal malaria sporozoite antigen in monkeys: adjuvant effects of aluminium hydroxide and non-pyrogenic liposomal lipid A .

Richards R L; Swartz G M; Schultz C; Hayre M D; Ward G S; Ballou W R; Chulay J D; Hockmeyer W T; Berman S L; Alving C R

Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Washington, DC 20307-5100.

Vaccine (ENGLAND) Dec 1989, 7 (6) p506-12, ISSN 0264-410X
Journal Code: 8406899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The immunogenicity of a recombinant protein (R32tet32) containing sequences from the tetrapeptide repeat region of the circumsporozoite protein of Plasmodium falciparum was enhanced by encapsulation in liposomes containing lipid A and adsorption of the liposomes with alum . The toxicities and efficacies of preparations containing different types and doses of lipid A were assessed by studying pyrogenicity in rabbits and adjuvanticity in monkeys. In each case liposomal lipid A was 25-fold to 200-fold less pyrogenic than free lipid A . Monophosphoryl lipid A , whether free or in liposomes, was the least pyrogenic of the three lipid A preparations tested. High antibody levels were obtained after immunization of rhesus monkeys with a formulation consisting of alum - adsorbed liposomes in which the liposomes contained R32tet32 and a strongly pyrogenic dose of native lipid A . Excellent antibody levels were also observed in monkeys immunized with a combination of R32tet32 encapsulated in alum - adsorbed liposomes containing non-pyrogenic doses of monophosphoryl lipid A and alum. The adjuvant effect was related to the dose of the lipid A in the liposomes, and the adjuvant effect was still strongly expressed despite suppression of the pyrogenic effect of lipid A . Antibody levels were considerably lower in monkeys immunized with liposomes lacking lipid A . It was concluded that a non-pyrogenic formulation of alum - adsorbed liposomes, in which the liposomes contained both lipid A and an encapsulated synthetic sporozoite antigen, shows considerable promise for inducing high titres of antibodies to sporozoites.

Record Date Created: 19900213

50/7/30 (Item 30 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05722493 88138469 PMID: 3277918
Liposomes, lipid A , and aluminum hydroxide enhance the immune response to a synthetic malaria sporozoite antigen.
Richards R L; Hayre M D; Hockmeyer W T; Alving C R
Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Washington, D.C. 20307-5100.
Infection and immunity (UNITED STATES) Mar 1988, 56 (3) p682-6, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A liposome-encapsulated cloned protein (R32tet32) containing sequences from the tetrapeptide repeat region of the circumsporozoite protein of Plasmodium falciparum sporozoites was examined for immunogenicity with rabbits and monkeys. Effects of adjuvants were tested by encapsulation of the antigen in liposomes either lacking or containing lipid A and adsorption with aluminum hydroxide (ALUM). When rabbits were immunized with R32tet32 alone, a primary antibody response was not seen and a secondary response did not appear until 32 to 36 weeks after boosting. Immunization with ALUM - adsorbed R32tet32 resulted in a minimal primary antibody response. A moderate secondary antibody response was detected within 2 weeks after boosting, but antibody levels decreased to preimmunization levels 8 weeks after boosting. When R32tet32 was encapsulated in liposomes containing lipid A , strong primary and secondary antibody responses were observed. Strong primary and secondary responses also were obtained when R32tet32 was encapsulated in liposomes either containing or lacking lipid A and the liposomes were adsorbed with ALUM . The strongest antibody response was obtained by immunization with ALUM - adsorbed liposomes containing lipid A and R32tet32, suggesting that the adjuvant effects of liposomes, lipid A , and ALUM were additive or synergistic.
Record Date Created: 19880330

50/7/31 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03610868 81167055 PMID: 7216495
Immunization of chimpanzees with hepatitis B virus-derived polypeptides.
Dreesman G R; Hollinger F B; Sanchez Y; Oefinger P; Melnick J L
Infection and immunity (UNITED STATES) Apr 1981, 32 (1) p62-7, ISSN 0019-9567 Journal Code: 0246127
Contract/Grant No.: HL 17269; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Previous studies established that the purified polypeptides derived from the 22-nm particles associated with hepatitis B surface antigen (HBsAg) produce both humoral and cellular immunity against HBsAg in guinea

pigs. Therefore, the two major polypeptides with molecular weights of 22,000 and 25,000 (P22 and P25, respectively) were isolated, adsorbed to an alum adjuvant , and used to immunize four nonimmune chimpanzees. A vigorous anti-HBs response was observed in all four animals after one inoculation of an alum - adsorbed polypeptide vaccine containing 40 micrograms of protein. After one to two booster inoculations, anti-HBs switched from being predominantly immunoglobulin M to the immunoglobin G class, indicating the establishment of immunological memory. Challenge of the vaccinated chimpanzees with 30,000 chimpanzee infectious doses of hepatitis B virus provided evidence for the efficacy of this vaccine. None of the four animals developed serological markers associated with an active hepatitis B infection, and no biochemical or histopathological changes of hepatitis were observed. A nonvaccinated control chimpanzee that was inoculated with the same hepatitis B virus material developed hepatitis B infection, confirming infectivity of the challenge inoculum.
Record Date Created: 19810623

50/7/32 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13065919 BIOSIS NO.: 200100273068
Vaccines.
AUTHOR: Momin Patricia Marie(a); Garcon Nathalie Marie-Josephe
AUTHOR ADDRESS: (a)Brussels**Belgium
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1240 (2):pNo Pagination Nov. 14, 2000
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The present invention provides vaccine compositions comprising an oil-in-water emulsion optionally with 3 De-O- acylated monophosphoryl lipid A and QS21. The vaccines compositions are potent inducers of a range of immune responses.

50/7/33 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12536429 BIOSIS NO.: 200000289931
Hepatitis B vaccine.
AUTHOR: Hauser Pierre(a); Garcon Nathalie Marie-Josephe Claude ; Desmons Pierre
AUTHOR ADDRESS: (a)Chaumont Gistoux**Belgium
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1227 (4):pNo pagination Oct. 26, 1999
MEDIUM: e-file.
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A novel vaccine formulation is provided, comprising a hepatitis B component, particularly hepatitis B surface antigen, in combination with aluminum phosphate and 3-O- acylated monophosphoryl lipid A .

50/7/34 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11522424 BIOSIS NO.: 199800303756
Liposomes containing lipid a serve as an aduvant for induction of antibody and cytotoxic T-cell responses against RTS,S malaria antigen.
AUTHOR: Richards Roberta L(a); Rao Mangala; Wassef Nabila M; Glenn Gregory M; Rothwell Stephen W; Alving Carl R
AUTHOR ADDRESS: (a)Dep. Membrane Biochem., Walter Reed Army Inst. Res., Washington, DC 20307-5100**USA
JOURNAL: Infection and Immunity 66 (6):p2859-2865 June, 1998
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Encapsulation of soluble protein antigens in liposomes was previously shown to result in processing of antigen via the major histocompatibility complex class I pathway, as evidenced by costaining of the trans-Golgi region of murine bone marrow-derived macrophages (BMs) by fluorophore-labeled liposomal antigen and by a trans-Golgi-specific fluorescent lipid. Evidence is presented here that free or liposome-encapsulated RTS,S, a particulate malaria antigen consisting of hepatitis B particles coexpressed with epitopes from the Plasmodium falciparum circumsporozoite protein, also was localized in the trans-Golgi after incubation with BMs, suggesting processing by the class I pathway. An in vivo cytotoxic T-lymphocyte (CTL) response was detected, however, only after immunization with RTS,S encapsulated in liposomes containing lipid A and not after immunization with free RTS,S or with RTS,S encapsulated in liposomes lacking lipid A. Therefore, intracellular delivery of antigen containing CTL epitopes to the Golgi of BMs does not necessarily result in a CTL response in vivo unless an additional adjuvant, such as liposomes containing lipid A, is utilized. Encapsulation of RTS,S in liposomes containing monophosphoryl lipid A (MPL) resulted in a dose-dependent enhancement of the NANP-specific immunoglobulin G (IgG) antibody response compared to that of free RTS,S. The IgG1 and IgG2a subclasses predominated after immunization with RTS,S encapsulated in liposomes containing MPL. These results demonstrate that encapsulation of a lipid-containing particulate antigen, such as RTS,S, in liposomes containing lipid A can enhance both humoral and cellular immune responses.

50/7/35 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11312628 BIOSIS NO.: 199800093960
Immunogenicity of Plasmodium falciparum circumsporozoite protein multiple antigen peptide vaccine formulated with different adjuvants.

AUTHOR: Le Thong P; Preston-Church L W; Corradin Giampietro; Hunter Robert L; Charoenvit Yupin; Wang Ruobing; De La Vega Patricia; Sacci John; Ripley-Ballou W; Kolodny Nelly; Kitov Svetlana; Glenn Gregory M(a); Richards Roberta L; Alving Carl R; Hoffman Stephen L
AUTHOR ADDRESS: (a)Dep. Membrane Biochem., Walter Reed Army Inst. Res., Washington, DC**USA
JOURNAL: Vaccine 16 (2-3):p305-312 Jan.-Feb., 1998
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Only low antibody levels were obtained from vaccinating human volunteers with single-chain peptide from the Plasmodium falciparum circumsporozoite protein (PfCSP). This resulted in modest protection against sporozoite challenge. In addition, HLA restriction limits the probability of synthesis of a vaccine effective for a diverse population. We report immunization studies with a multiple antigen peptide (MAP) system consisting of multiple copies of a B-cell epitope from the central repeat region of the PfCSP in combination with a universal T-cell epitope, the P2P30 portion of tetanus toxin. This MAP4(NANP)6P2P30 vaccine was highly immunogenic in four different strains of mice when used with various safe and nontoxic adjuvants. When this MAP vaccine was encapsulated in liposomes with lipid A and adsorbed to aluminum hydroxide and given three times at 4-week intervals, the resultant antibody prevented 100% of sporozoites from invading and developing into liver stage infection. This high degree of immunogenicity of MAP4(NANP)6P2P30 vaccine formulated in liposomes, lipid A and aluminum hydroxide provides the foundation for consideration of human trials with this formulation.

50/7/36 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09569947 BIOSIS NO.: 199598024865
Synergistic association of adjuvants QS21 and MPL for induction of cytolytic T lymphocytes and T helper responses to recombinant protein antigens.
AUTHOR: Bastin C; Hermand P; Francotte M; Garcon N ; Slaoui M; Pala P
AUTHOR ADDRESS: SmithKline Beecham Biol., Rixensart**Belgium
JOURNAL: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy 34 (0):p26 1994
CONFERENCE/MEETING: 34th Interscience Conference on Antimicrobial Agents and Chemotherapy Orlando, Florida, USA October 4-7, 1994
RECORD TYPE: Citation
LANGUAGE: English

50/7/37 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08727316 BIOSIS NO.: 199395016667
Immunogenicity of recombinant core particles of hepatitis B virus containing epitopes of human immunodeficiency virus 1 core antigen.

AUTHOR: Ulrich R(a); Borisova G P; Gren E; Berzin I; Pumpen P; Eckert R; Ose V; Siakkou H; Gren E J; et al
AUTHOR ADDRESS: (a)Inst. Virol., Charite, Schumannstrasse 20/21, D-1040 Berlin**French Guiana
JOURNAL: Archives of Virology 126 (1-4):p321-328 1992
ISSN: 0304-8608
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A Gag protein segment of human immunodeficiency virus 1 (HIV-1) has been fused to a C terminally truncated core antigen of hepatitis B virus (HBcAg) using an E. coli expression system. Fusion of 90 amino acids of HIV-1 Gag protein to HBcAg still allowed the formation of capsids presenting on their surface epitopes of HIV-1 core protein, whereas fusion of 317, 189, or 100 amino acids of Gag prevented self-assembly of chimeric particles. Mice immunized with recombinant particles emulsified with Freund's complete adjuvant (CFA) or aluminium hydroxide developed high anti-HBcAg titers. However, anti-HIVp24 antibodies were detected only in mice inoculated with immunogen emulsified with CFA.

50/7/38 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07750991 BIOSIS NO.: 000092064712
LARGE-SCALE PURIFICATION OF INACTIVATED HEPATITIS A VIRUS BY CENTRIFUGATION IN NON-IONIC GRADIENTS
AUTHOR: DUBOIS D R; ECKELS K H; TICEHURST J; BINN L N; TIMCHAK R L; BARVIR D A; RANKIN C T; O'NEILL S P
AUTHOR ADDRESS: DEP. BIOL. RES., BUILD. 506, FOREST GLEN SECT., WALTER REED ARMY INST. RES., WASHINGTON, D.C. 20307-5100, USA.
JOURNAL: J VIROL METHODS 32 (2-3). 1991. 327-334. 1991
FULL JOURNAL NAME: Journal of Virological Methods
CODEN: JVMED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Formalin-inactivated hepatitis A virus (HAV) can be purified for vaccine preparation by centrifugation in Renografin-76 (diatrizoate meglumine and diatrizoate sodium) gradients. Both continuous-flow rate-zonal and isopycnic methods were used for the separation of a major antigen component from minor antigen and host protein. The major antigen component, which appeared to contain complete virions by electron microscopy, could be recovered from gradients and accounted for approximately one third of the total antigen in the starting material. The HAV-specific purified antigen could be enriched 200-300-fold by either centrifugation procedure. The purified HAV antigen , when adsorbed to alum and inoculated into mice, was found to be highly immunogenic.

50/7/39 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11327543 EMBASE No: 2001341053
Targeting polymerised liposome vaccine carriers to intestinal M cells
Ann Clark M.; Blair H.; Liang L.; Brey R.N.; Brayden D.; Hirst B.H.
B.H. Hirst, Department of Physiological Sciences, Medical School, University of Newcastle, Newcastle upon Tyne NE2 4HH United Kingdom
AUTHOR EMAIL: barry.hirst@ncl.ac.uk
Vaccine (VACCINE) (United Kingdom) 12 OCT 2001, 20/1-2 (208-217)
CODEN: VACCD ISSN: 0264-410X
PUBLISHER ITEM IDENTIFIER: S0264410X01002584
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 44

Due to their transcytotic capability, intestinal M cells may represent an efficient potential route for oral vaccine delivery. We previously demonstrated that the lectin Ulex europaeus agglutinin 1 (UEA1, specific for alpha-l-fucose residues) selectively binds to mouse Peyer's patch M cells and targets 0.5 mum polystyrene microparticles to these cells. Using a gut loop model we now demonstrate that covalently -membrane- bound UEA1 similarly targets polymerised liposomes (Orasomes(TM), approximately 200 nm diameter), potential biocompatable oral vaccine delivery vehicles, to mouse M cells. Targeting was inhibited by alpha-l-fucose while the co-entrapped adjuvant, monophosphoryl Lipid A (MPL(R)), failed to exert any detrimental effect on UEA1-mediated M cell targeting. Lectin-mediated M cell targeting may thus permit the efficacy of mucosal vaccines to be enhanced if cellular relationship between particle binding and immune outcome can be established.

50/7/40 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11291836 EMBASE No: 2001306730
Induction of cross clade reactive specific antibodies in mice by conjugates of HGP-30 (peptide analog of HIV-1SUBSF2 p17) and peptide segments of human beta-2-microglobulin or MHC II beta chain
Zimmerman D.H.; Lloyd J.P.; Heisey D.; Winship M.D.; Siwek M.; Talor E.; Sarin P.S.
D.H. Zimmerman, CEL-SCI Corporation, 8229 Boone Blvd, Vienna, VA 22182 United States
AUTHOR EMAIL: dzimmerman@cel-sci.com
Vaccine (VACCINE) (United Kingdom) 14 SEP 2001, 19/32 (4750-4759)
CODEN: VACCD ISSN: 0264-410X
PUBLISHER ITEM IDENTIFIER: S0264410X0100247X
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 66

HGP-30, a 30 amino acid synthetic peptide homologous to a conserved region of HIV-1SUBSF2 p17 (aa86-115), has previously been shown to elicit both cellular and humoral immune responses when conjugated to KLH and adsorbed to alum . However, the free HGP-30 peptide is not immunogenic in animals. In order to improve the immunogenicity of HGP-30, peptide conjugates consisting of a modified HGP-30 sequence (m-HGP-30/aa82-111) and

a peptide segment, residues 38-50, of the MHC I accessory molecule, human beta-2-microglobulin (beta-2-M), referred to as Peptide J, or a peptide from the MHC II beta chain (peptide G) were evaluated in mice. The effects of carriers and adjuvants on serum antibody titers, specificities to various HIV-1 clade peptides similar to HGP-30 and isotype patterns were examined. Peptides J or especially G conjugated to modified-HGP-30 (LEAPS 102 and LEAPS 101, respectively) generated comparable or better immune responses to modified HGP-30 than KLH conjugates as judged by the induction of: (1) similar antibody titers; (2) broader HIV clade antigen binding ; and (3) antibody isotype response patterns indicative of a TH1 pathway (i.e. increased amounts of IgG2a and IgG2b antibodies). The ISA 51 and MPL(R)-SE adjuvants induced higher antibody responses than alum, with the ISA 51 being more potent. Immune responses to LEAPS 102, as compared to LEAPS 101, were weaker and slower to develop as determined by antibody titers and cross clade reactivity of the antibodies induced. Compared to KLH conjugates which induced significant anti-KLH antibody titers, minimal antibody responses were observed to peptide G, the more immunogenic conjugate, and peptide J. These results suggest that modified HGP-30 L.E.A.P.S. constructs may be useful as HIV vaccine candidates for preferential induction of TH1 directed cell mediated immune responses.

50/7/41 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

07305990 EMBASE No: 1998193359
Aluminum compounds as vaccine adjuvants
Gupta R.K.
R.K. Gupta, Wyeth-Lederle Vaccines and Pediatr., 401 North Middletown Road, Pearl River, NY 10965 United States
Advanced Drug Delivery Reviews (ADV. DRUG DELIV. REV.) (Netherlands) 06 JUL 1998, 32/3 (155-172)
CODEN: ADDRE ISSN: 0169-409X
PUBLISHER ITEM IDENTIFIER: S0169409X98000088
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 168

Aluminum compounds are the only adjuvants used widely with routine human vaccines and are the most common adjuvants in veterinary vaccines also. Though there has been a search for alternate adjuvants, aluminum adjuvants will continue to be used for many years due to their good track record of safety, low cost and adjuvanticity with a variety of antigens. For infections that can be prevented by induction of serum antibodies, aluminum adjuvants formulated under optimal conditions are the adjuvants of choice. It is important to select carefully the type of aluminum adjuvant and optimize the conditions of adsorption for every antigen since this process is dependent upon the physico-chemical characteristics of both the antigens and aluminum adjuvants . Adsorption of antigens onto aluminum compounds depends heavily on electrostatic forces between adjuvant and antigen. Two commonly used aluminum adjuvants, aluminum hydroxide and aluminum phosphate have opposite charge at a neutral pH. The mechanism of adjuvanticity of aluminum compounds includes formation of a depot; efficient uptake of aluminum adsorbed antigen particles by antigen presenting cells due their particulate nature and optimal size (< 10 mum);

and stimulation of immune competent cells of the body through activation of complement, induction of eosinophilia and activation of macrophages. Limitations of aluminum adjuvants include local reactions, augmentation of IgE antibody responses, ineffectiveness for some antigens and inability to augment cell-mediated immune responses, especially cytotoxic T- cell responses.

50/7/42 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

06518120 EMBASE No: 1996183312
Effects of aluminum adjuvant compounds, tweens, and spans on the stability of liposome permeability
Muderhwa J.M.; Wassef N.M.; Spitler L.E.; Alving C.R.
Department of Membrane Biochemisry, Walter Reed Army Institute Research,Washington, DC 20307-5100 United States
Vaccine Research (VACCINE RES.) (United States) 1996, 5/1 (1-13)
CODEN: VAREE ISSN: 1056-7909
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The ability of liposomes to retain their integrity and to serve as a permeability barrier for encapsulated antigen, properties that are theoretically important for optimal adjuvant activity, was breached when the liposomes were adsorbed to aluminum hydroxide gels. Stability of liposomal permeability was assessed by using either glucose or prostate specific antigen (PSA) as an encapsulated aqueous marker. Liposomes composed of dimyristoyl phosphatidylcholine, dimyristoyl phosphatidylglycerol, cholesterol, and lipid A were destabilized following adsorption to aluminum adjuvant compounds, resulting in release of trapped glucose or encapsulated PSA, respectively. The release, which increased linearly with time in a temperature-dependent manner, was more than 3-fold higher in the case of encapsulated PSA than with trapped glucose. It was independent of the phospholipid structure and the liposomal surface charge. The destabilization of aluminum-adsorbed liposomes was reversed in a concentration-dependent manner by incorporation of fatty acid esters of polyoxyethylene sorbitan (Tweens), but not by fatty acid esters of sorbitan (Spans), into the liposomal lipid bilayer. We conclude that Tweens can serve as useful constituents of liposomes for stabilizing liposomes when they are present in complex mixtures of adjuvants.

50/7/43 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

06440901 EMBASE No: 1996095517
Adjuvant properties of non-phospholipid liposomes (Novasomes(R)) in experimental animals for human vaccine antigens
Gupta R.K.; Varanelli C.L.; Griffin P.; Wallach D.F.H.; Siber G.R.
Massachusetts Public Health Biologic, Laboratories, State Laboratory Institute,Boston, MA 02130 United States
Vaccine (VACCINE) (United Kingdom) 1996, 14/3 (219-225)
CODEN: VACCD ISSN: 0264-410X
DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Non-phospholipid liposomes composed of dioxyethylene cetyl ether, cholesterol and oleic acid were evaluated as adjuvants with human vaccine antigens, tetanus toxoid (TT) and diphtheria toxoid (DT), in mice and rabbits. Antigens encapsulated in or mixed with liposomes elicited antitoxin levels similar to those elicited by antigens given with Freund's adjuvant or adsorbed onto aluminum phosphate . All liposomal antigen preparations, antigen given with Freund's adjuvant or adsorbed onto aluminum phosphate , elicited significantly higher IgG antibodies and antitoxin levels than soluble antigens in mice after a single injection and in rabbits after each of three injections. TT encapsulated in liposomes elicited sustained anti-TT IgG antibody levels in mice after a single injection as compared to TT mixed with liposomes. TT mixed with or encapsulated within liposomes containing monophosphoryl lipid A /squalene or squalene alone, as well as aluminum phosphate adsorbed TT elicited greater primary responses in mice than TT mixed with or encapsulated within plain liposomes. Liposomal TT preparations produced a slightly higher anamnestic response in mice than aluminum phosphate adsorbed TT. Subclass analysis of anti-TT antibodies showed that the majority of the antibodies belong to IgG1 subclass. Liposomal TT preparations, particularly those with encapsulated monophosphoryl lipid A /squalene or squalene alone, consistently elicited higher levels of anti-TT IgG2a and IgG2b than aluminum phosphate adsorbed or soluble TT. None of the preparations elicited IgG3 or IgM antibodies. It appears that non-phospholipid liposomes are as potent adjuvants as the currently employed adjuvant for human vaccines (aluminum phosphate) or a benchmark adjuvant for experimental immunology (Freund's adjuvant), and may be able to modulate the immune response towards the Th1 type.
?logoff hold